



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,145	08/04/2003	Chew Kiat Heng	NAA 0018 PA/41049.20	5097
23368	7590	06/28/2007		
DINSMORE & SHOHL LLP ONE DAYTON CENTRE, ONE SOUTH MAIN STREET SUITE 1300 DAYTON, OH 45402-2023			EXAMINER WHALEY, PABLO S	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 06/28/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/634,145	Applicant(s) HENG, CHEW	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 and 17-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' remarks, filed 04/17/2007, have been fully considered. The following rejections and/or objections are maintained, newly applied, or withdrawn for the reasons set forth below. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims 1-15 and 17-30 are herein under examination. Claims 28-30 are newly added. This application contains claim 16 drawn to an invention nonelected with traverse in the response filed 01/31/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-15, 17-19, and 22-26 remain rejected and newly added claims 28-30 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter.

Applicant's arguments, filed 4/17/2007, are persuasive in view of the amendment(s) to instant claim 27, which now appears to result in storing weights to at least one computing device, and instant claim 20, which now recites a system comprising at least one computing device. This rejection is hereby withdrawn for claims 20 and 27.

Applicant's arguments, filed 4/17/2007, that claims 1-15, 17, 18, 19, and 21-26 now recite a "data transformation" are not deemed to be persuasive for the following reasons. This rejection is maintained for the reasons set forth below.

According to the revised Guidelines, a claimed invention directed to a statutory process must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))]. The revised Guidelines also state that the focus is "not on whether the steps taken to achieve a particular result are useful, tangible, and concrete, but rather on whether the final result achieved by the claimed invention is useful, tangible, and concrete."

Art Unit: 1631

Claims 1-15, 17-19, 22-26 and 28-30 are now directed to a computer-implemented method of determining a statistical model for predicting disease risk. Claim 1 has been amended to include the limitation of a computing device, however the Examiner maintains that no steps directed to a physical transformation of matter or recited in the claims. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). However, the instant claims still result in optimizing parameters, which encompasses a non-physical method step that may be practiced inside of a computer (i.e. *in-silico*). For the above reasons, the instant claims lack a "tangible" result and thus do not recite more than a 35 U.S.C. 101 judicial exception. Therefore, the instant claims are not statutory.

This rejection could be overcome by amending the claims to recite a step wherein the result of the claimed method is communicated to a user (i.e. real world result), graphically displayed, or output (e.g. to a user, to a memory, or to another computer) or by amending the claims to include a step of a physical transformation of matter (e.g. assay). For an updated discussion of statutory considerations, see the revised Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV (Latest Revision August 2006).

NEW MATTER

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

Art Unit: 1631

relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 now recites a step of optimizing parameters of a candidate model by fitting, wherein said fitting comprises "calculating for each of said sets, a deviate of a predicted risk from an indicator of disease status for that set, said predicted risk predicted using said candidate model and non-genetic data" and "calculating a sum of weighted deviates for all of said sets, wherein each deviate is weighted in said sum by the weight associated with that set for which said each deviate has been calculated." In the response filed 04/17/2007, applicant does not point to support for these newly recited limitations. The Examiner has not found support for these limitations in the specification, and these limitations are not present within the scope of the original claims as filed. As the newly recited limitations are not supported by the originally filed claims or disclosure, the claims are rejected for reciting new matter. This rejection is necessitated by amendment.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *These rejections are necessitated by amendment.*

Claims 1, 27, and 28 are rejected for the following reasons. Claims that indirectly or directly depend from claims 1 and 28 are also rejected due to said dependence.

Art Unit: 1631

Claim 1 now recites "collecting, at least one computing device, a plurality of data sets." It is unclear whether applicant intends for devices or data sets to be collected. Clarification is requested via clearer claim language.

Claim 1 now recites "storing at least one computing device a candidate statistical model." It is unclear whether applicant intends for models or a computing device to be stored. Clarification is requested via clearer claim language.

Claim 3 now recites "each weighted deviate is a product of the corresponding weight and a function of the corresponding deviate." It is unclear in whether said weighted deviate is a product of said corresponding weight and a function, or whether said weighted deviate is both a product and a function. Clarification is requested via clearer claim language.

Claim 13 now recites "adjustment factor indicative of an extent to which the member is associated with said ...weights is representative of members." The term "an extent" is a relative term of degree, therefore it is unclear as to what "extent" adjustment factors indicate the weights representative of members. Clarification is requested.

Claim 27 now recites "storing, at least one computing device, said weight." It is unclear whether applicant intends for a computing device or said weight to be stored. Clarification is requested via clearer claim language.

Claim 28 now recites "storing, at least one computer, a plurality of statistical models." It is unclear whether applicant intends for models or a computing device to be stored. Clarification is requested via clearer claim language.

CLAIM REJECTIONS - 35 USC § 102

Claims 1, 2, 3, 9-11, 13, and 19-21 were rejected under 35 U.S.C. 102 (b) as being anticipated by Schoonjans (MedCalc, www.medcalc.be/manual/cox-regression.php , Copyright 1993, p.1-6).

Applicant's arguments, filed 04/17/2007, that Schoonjans does not teach "predicting risks using a candidate model and non-genetic data, and optimizing the model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets" are persuasive. This rejection is hereby withdrawn.

Claims 1, 2, and 10 were rejected under 35 U.S.C. 102 (b) as being anticipated by Fisher et al. (Annu. Rev. Public Health, 1999, 20, p.145-157).

Applicant's arguments, filed 04/17/2007, that Fisher et al. does not teach "predicting risks using a candidate model and non-genetic data, and optimizing the model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets" are persuasive. This rejection is hereby withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 3, 9, 19, 20, 21, 23, and 28-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Dodds et al. (US 6,287,254; Issued: Sept. 11, 2001), in view of Luciano et al. (US 6,063,028; Issued May 16, 2000). ***This rejection is necessitated by amendment.***

Dodds et al. teach a veterinary diagnostic method, system and apparatus of health profiling of an animal subject [Abstract]. More specifically, Dodds et al. teach the following aspects of the instantly claimed invention:

- Dodds et al. teach the use of phenotypic data [Col. 1, lines 50-65] and genotypic data [Col. 2, lines 40-55] and [Col. 11], as in claims 1, 23, 28.
- obtaining genetic data associated with a selected animal; obtaining phenotype health assessment data associated with a selected animal (i.e. non-genetic data); combining

the genetic data and the phenotype health assessment data to determine a relationship between the genetic data and the phenotype health assessment data using a computer program [Ref. Claim 1], as in claims 1 and 9.

- selecting from data relating to temperament of animal, lifespan of animal, or physiologic or genetic marker for autoimmune thyroiditis or thyroid dysfunction of the selected animal [Ref. Claim 1], which equate to indicators of disease status, as in claim 1.

Dodds et al. also teach a computer system [Fig. 1] for inputting data into a genetic database and phenotypic database, and other databases, storing the data in these databases, analyzing the data in a relational sense from the different databases, and retrieving the data from these databases [Col. 7, ¶ 4], as in claims 20 and 21. Dodds et al. also teach phenotype and genotype databases wherein data is divided into particular groupings [Col. 21, ¶ 3 and 4], a genetic marker database [Col. 21, ¶ 6], and an algorithm that relates coefficients and predictability data (i.e. criteria) from the above data to determine an output [Col. 22, ¶ 3], which the Examiner has broadly interpreted as a teaching for claim 23.

Dodds et al. do not specifically teach determining weights associated with a model or optimizing model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets, as in claims 1, 2, 3, 19, 20, 21, and 28-30. However, Dodds et al. teach the use of genetic and non-genetic data for building computer driven statistical models for predicting the occurrence of specific diseases [Col. 7, ¶ 3].

Luciano et al. teach a method which includes the optimization of model parameters that yield the best fit to the data through minimization of squared error, which is an implicit teaching for calculation of deviates [Col. 15, ¶ 2] and [[Col. 17, lines 45-55], as in claim 1. More

Art Unit: 1631

specifically, Luciano et al. teach optimization through iterative modification of parameters to minimize the discrepancy between predicted and actual values to find the best model parameters [Col. 15, ¶ 4], and equations for calculating optimized model parameters based on summations of weighted deviations that incorporate estimated and actual data [See Fig. 3-8 below]. Luciano et al. teach the limitations of claims 1, 2, 3, 19, 20, 21, and 28-30.

FIG. 3-8

$$L = \int_0^T \sum_{ik} \left\{ \left(X_{ik} - \hat{X}_{ik} \right)^2 + \mu_{ik} \left(\hat{X}_{ik} - f \left(\hat{X}_{ik} \right) \right) \right\} dt + K \sum_j P_j^2$$

estimated ⁸²⁰

actual

L = Error term k = patients i = symptoms j = parameter x = data	Obtain optimized parameters - fit patient data - train on entire recovery period - minimize error term L - gradient descent on parameters
---	--

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the disease risk prediction method taught by Dodds et al. with the additional model optimization steps taught by Luciano et al., as Dodds et al. suggest continually updating statistical models to enhance predictive ability [Dodds et al., Col. 7, ¶ 3]. One of ordinary skill in the art would have been motivated to combine the above teachings in order to

Art Unit: 1631

develop an optimized model for improved disease risk prediction [Luciano et al., Col. 5, ¶ 1], resulting in the practice of the instant claimed invention. One of skill in the art would have had a reasonable expectation of successfully combining the above teachings both Dodds et al. and Luciano et al. clearly teach the use of statistical techniques including regression analysis [Dodds et al. Col. 7, ¶ 3].

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Dodds et al. (US 6,287,254; Issued: Sept. 11, 2001), in view of Tibshirani (STATISTICS IN MEDICINE, 1997, Vol. 16, p.385-395) and Nelson et al. (J Clin Epidemiol, 1998, Vol. 51, No. 3, pp. 199-209). ***This rejection is necessitated by amendment.***

Dodds et al. teach a veterinary diagnostic method, system, and apparatus for predicting health in animal subjects [Abstract], as set forth above.

Dodds et al. do not specifically teach determining weights associated with a model or optimizing model parameters by minimizing the sum of weighted deviates, where the deviates are weighted by corresponding weights that reflect genetic data associated with the respective data sets, as in claims 1-3, 9-15, 17-22, and 27-30. Dodds et al. also do not specifically teach steps directed to recursive division of data, as in claims 4-7 and 24-26.

Tibshirani teaches a computer-implemented method for determining variables for a Cox proportional-hazard model [Abstract]. More specifically, Tibshirani teaches the following aspects of the instantly claimed invention:

- A plurality of data sets associated with lung and liver cancer studies comprising Karnofsky scores, age, sex, state of disease, cell type, treatment, etc. [p.387] and

[p.389], which the Examiner has broadly interpreted as teachings for 'indicator of disease status', and 'non-genetic' data, as in claim 1, 15-18, 28-30.

- A Cox statistical model for calculating risk and dependent on a plurality of parameters comprising time, predictor values, and baselines functions [Section 1, Equations 1 and 2], as in claims 1, 8, 10, 11, 13, 28-30.
- Notation of partial likelihood functions comprising standardized "x" variables that are indexed for association with population members and weighted by N [p.386, ¶ 2], which the Examiner has broadly interpreted as an 'adjustment factor' as in claim 14 and 27.
- An minimization of model parameter via an argmin function (i.e. target function) [p.386, ¶ 1] and an iterative "weighted" least squares algorithm used for minimization of model parameters [p.386, Section 2], as in claim 1.
- Calculating of deviations in data sets using seventeen variables and using full, stepwise, and Lasso models (i.e. which incorporates minimized weighted values as described in Section 2) for data simulations [p.390, Table I] and [p.391, Section 5.2 and Fig. 2], as in claim 1, 20, and 28-30.
- Computation of model parameters using quadratic programming techniques [p.386, Section 2], which is an implicit teaching for computer devices, computer executable instructions, and computer readable mediums, as in claims 1 and 21.
- Calculation of mean squared error and relative risk scores for grouped model parameters and for optimized models (i.e. Lasso), including disease status (x_{17}) [p.389 and Table I], which is an implicit teaching for a difference calculation, as in claim 1.
- Clinical examples wherein data indicative of a plurality of factors is grouped (i.e. by case reference number, sex, age, etc.) according to seventeen variables, wherein groups

include values of 0 and 1, and wherein missing values are discarded (i.e. imputing missing data) [p.389, ¶ 1], as in claims 12, 22.

- Comparison of models after simulation for selection of optimum model, wherein one model uses a different number of parameters [Table I], and Lasso model outperforming the rest and selecting appropriate number of coefficients [Table 1] and [p.391, Section 5.1], as in claims 28-30.

Nelson et al. teach the use of recursive partitioning to produce classification trees, wherein subjects are assigned to subsets according to a set of predictor variables [Abstract]. Critical limitations that relate to the instantly claimed invention include: using recursive division of data based on specific criteria for data classification into terminal subsets [Fig. 1], as in claims 24-26. Nelson et al. also teach a splitting criterion (i.e. Gini index) to identifying variable that minimize variance between case (i.e. disease) and control groups (i.e. reference), wherein the Gini index (i.e. weight) is calculated for each group and comprises values between zero and one [p.207 and 208, Appendix A] and [Fig. 1], as in claims 4-7.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the disease risk prediction method taught by Dodds et al. with the additional use of classification trees based on recursive partitioning as taught by Nelson et al., and the Cox hazard model taught by Tibshirani, as the use of recursive partitioning with disease prediction models is well known [Nelson et al., p.201, Col. 1, ¶ 1] and as Dodds et al. suggest continually updating statistical models to enhance predictive ability [Dodds et al., Col. 7, ¶ 3]. One of ordinary skill in the art would have been motivated to combine the above teachings in order to use optimized model for improved disease risk prediction [Tibshirani, Abstract] and recursive partitioning is well known for improving the accuracy of disease prediction [Nelson et

Art Unit: 1631

al., p.201, Col. 1, ¶ 1], resulting in the practice of the instant claimed invention. One of skill in the art would have had a reasonable expectation of successfully combining the above teachings as Dodds et al. clearly teaches the use of statistical techniques including regression analysis [Dodds et al. Col. 7, ¶ 3] and as Tibshirani and Nelson et al. also teach methods of regression analysis [p.204, Col. 1, ¶ 2].

CONCLUSION

No claims are allowed.

Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

Art Unit: 1631

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley
Patent Examiner
Art Unit 1631
Office: 571-272-4425
Direct Fax: 571-273-4425

MICHAEL BORIN, PH.D.
PRIMARY EXAMINER

